Long-Term Excess Mortality after Aneurysmal Subarachnoid Hemorrhage

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Thesis

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Tiivistelmä – Referat – Abstract

Objective

There is high case-fatality rate and loss of productive life-years related to aneurysmal subarachnoid hemorrhage (aSAH) but little data on long-term survival of SAH patients. We aim to evaluate long-term excess mortality and related risk factors after aSAH.

Methods

One year survivors (n=3080) after aSAH from Department of Neurosurgery in Helsinki between 1980 and 2007 were reviewed for this retrospective follow-up study. Follow-up started one year after SAH and continued until death or the end of 2008 (36 960 patient-years). Mortality and relative survival ratio (RSR) were compared with matched general population.

Results

After 20 years, survivors of aSAH showed 18% excess mortality compared to general population. Risk factors included: old age; poor preoperative clinical condition; conservative aneurysm treatment; multiple aneurysms; and unfavourable clinical outcome at 3 months.

Conclusion

Even after initially favourable recovery, patients with aSAH experience excess mortality in the long run. Cardiovascular and cerebrovascular diseases are prominent in this population.

(150)

Avainsanat – Nyckelord – Keywords

Excess Mortality, Intracranial Aneurysm, Long-Term Mortality, Mortality, Outcome, SAH, Subarachnoid Hemorrhage

Säilytyspaikka – Förvaringställe – Where deposited

Muita tietoja – Övriga uppgifter – Additional information

1 Introduction

Subarachnoid hemorrhage (SAH), caused by ruptured cerebral aneurysm, is a serious disease with high mortality (1,2). The most characteristic symptom of subarachnoid hemorrhage is sudden and severe headache, deterioration of consciousness, nausea and vomiting (3). For unknown reasons the incidence of subarachnoid hemorrhage is by far higher in Finland (21 / 100 000 person-years) and Japan than in most other parts of the world (8 / 100 000 person-years) (4). Yearly about 1000 Finns suffer from subarachnoid hemorrhage and almost half of them die, 15% even before reaching any medical care (2). Patients who survive the initial hours after the bleeding, three major neurological complications can threaten: rebleeding, delayed brain ischemia and hydrocephalus, all of which cause severe morbidity and mortality during the first months after SAH (5-7).

The case- fatality rate for aneurysmal SAH is still close to 50% even though it has improved slowly over time thanks to better diagnostic tools and improved medical and surgical treatment strategies (2). Even nowadays, although only 5-10% of all strokes are caused by subarachnoid hemorrhage, the loss of productive life years is similar to that for cerebral infarction or intracerebral hemorrhage, since SAH strikes at fairly young age and is often fatal (8). Half of the patients are younger than 55 years (8). Despite the known high case-fatality rate of SAH up to 6 months, there is only very little data on what happens to SAH patients later on. Is their life expectancy similar to that of somebody who has never had SAH or are they more prone to develop other medical conditions leading to morbidity and mortality? The aim of this study is to find out if there is excess mortality among patients with aneurysmal SAH in the long run, compared to matched general population.

There are only few publications on long-term survival of SAH patients and their conclusions are slightly contradicting (1,9-12). Most studies have shown at least some excess mortality among SAH patients when compared to matched general population (1,9,11,12), whereas other results suggest quite the opposite (10). Knowledge on prospects of long-term survival and recovery after aneurysmal SAH is important for the patients, their families as well as for those deciding on the use of health economy resources. More information is needed concerning long-term mortality of SAH patients and

the risk factors related to impaired survival. Some of the risk factors may be treatable and this way the prognosis may be improved. For example, are multiple aneurysms predisposing factor for long-term mortality? Some patients are more prone to develop multiple aneurysms but it is not known whether these patients should be followed-up or treated more actively than those with just a single aneurysm.

2 Patients and Methods

Patients and Helsinki Cerebral Aneurysm Research- Data base

This is a single institution, retrospective follow-up study. There were altogether 4228 SAH patients treated between 1980 and 2007 at Department of Neurosurgery at Helsinki University Central Hospital, the sole provider of neurosurgical services for the catchment population of 1.8 million people living in Southern Finland. The clinical and radiological data of these patients was reviewed from Helsinki Cerebral Aneurysm Research- Data base; HeCARe- Data base, the largest data-base of its kind in the world. Patients with other than saccular aneurysms, foreign patients and patients treated primarily at other neurosurcigal centers (n=270) were excluded. Of the remaining 3958 saccular aneurysm patients treated between years 1980 and 2007, those patients, who survived a minimum of one year after the initial SAH were included in this study. There were 9 patients who survived but were lost from follow-up within the first year after SAH. There were 3080 patients forming the final study sample. Characteristics of these 3080 subarachnoid hemorrhage patients are shown in Table 1. The mean age at the incidence of SAH was 49 (range 1-88). For women the mean age was 51 and for men 46 years.

Follow-Up Data

Follow-up period started one year after the initial SAH and continued until death or the end of the year 2008. The diagnosis of SAH was based on computed tomography (CT) and lumbar puncture. The ruptured aneurysm was identified with digital subtraction angiography (DSA), CT angiography (CTA) or MR angiography (MRA). Time of death or vital status at the end of the year 2008 was obtained from the Population Register Center, which contains this information on all residents in Finland. Patients' initial clinical condition upon arrival at the hospital was described using Hunt & Hess (HH) and World Federation of Neurosurgical Societies (WFNS) grading scales (13,14). For the purpose of data analysis, patients were assigned either to active or conservative treatment group based on

the treatment they received. Treatment was considered conservative if the patient did not receive any kind of neurosurgical operative or endovascular intervention at any point during the whole follow-up period. Clinical condition at 3 months after the onset of SAH was evaluated using Glasgow outcome score (GOS) (15). The total follow-up time was 36 960 patient-years with median follow-up of 12 years per patient (range 1–29 year(s)).

Table 1

Characteristics of 3080 aneurysmal subarachnoid hemorrhage patients who survived a minimum of one year and were treated in Helsinki University Hospital between 1980 and 2007.

	Total
Sex	
Female	1700 (55%)
Male	1380 (45%)
Number of aneurysms	
1	2177 (71%)
2	590 (19%)
3	211 (7%)
4	68 (2%)
>4	34 (1%)
Location of ruptured aneurysm	
ICA	593 (19%)
MCA	1047 (34%)
AcomA & A1	1094 (36%)
Pericallosal artery	138 (5%)
Posterior circulation	206 (7%)
Active treatment	
Yes	3034 (99%)
No	46 (1%)

Preoperative HH	*Total*
1	736 (24%)
2	1069 (35%)
3	692 (23%)
4	483 (16%)
5	99 (3%)
Preoperative WFNS	
1	1827 (59%)
2	561 (18%)
3	160 (5%)
4	335 (11%)
5	196 (6%)
GOS at 3 months	
5 Good Recovery	1404 (50%)
4 Moderate Disability	889 (32%)
3 Severe Disability	483 (17%)
2 Persistent vegetative state	23 (1%)
1 Death	0 (0%)
Vital status at the end of follow-up	
Alive	2367 (77%)
Dead	713 (23%)

Statistical Methods

Excess mortality describes death that occurs before the average life expectancy for a person compared to other people with similar demographic characteristics. To measure excess mortality in this study a relative survival ratio (RSR) was calculated by dividing the observed survival of treated SAH patients by the expected survival. The expected survival was derived, using the Ederer II method (16), from the expected survival of the comparable general Finnish population matched with respect to age, sex, calendar time and place of residence. This data concerning comparable Finnish population was obtained from Statistics Finland. The 95% confidence intervals (CI) for annual RSR and cumulative relative survival estimates were calculated by assuming normal distribution. Statistical analysis has been carried out using SAS software (SAS Institute, Cary NC).

Ethical Aspects

This study has been carried out following good ethical manner. It has been approved by the Ethics Committee of the Helsinki University Central Hospital, Dnro: 469/E0/04.

3 Results

Mortality

Mortality during the first year after aneurysmal SAH

At the beginning of the follow-up, one year after the SAH, there were 3080 (78%) patients alive. 869 (22%) patients had died during the first year. In 94% of them the primary SAH was the cause of death. Most of the patients who died during the first year (n=626, 72%) were in poor clinical condition (Hunt & Hess grades 4-5) on admission. Of all the patients who died during the first year, 87% died within the first 3 months. Due to expected poor prognosis, only 58% of the poor grade patients were treated actively.

Causes of Death and Recurrent SAH

During the follow-up, 713 patients (23%) died. Table 2 shows the causes of death in relation to follow-up periods. There were altogether 122 deaths caused by SAH over the whole time period. Majority of them (n=87, 71%) were related to the initial SAH. Re-bleeding before treatment or rebleeding from previously treated aneurysm was cause of death in 18 patients and 17 died due to rupture of another aneurysm. The incidence for lethal recurrent SAH was 95 per 100 000 person-years, which is about three times the risk of getting SAH as a general Finnish adult (incidence 35/100 000) (17).

Among the study group, the patients who survived a minimum of one year after SAH, the mean age at death was 65 (median 66; range 23- 90). The most common causes of death were cardiovascular disease (26%) and cancer (22%). Patients younger than 65 years also had cardiovascular disease as the leading cause of death (24%). Deaths caused by cerebrovascular disease were also common in our study group (15% for ≥ 65 years , 8% < 65 years).

Table 2

Causes of death of the 713 SAH patients who died during follow-up.

	Time from the beginning of follow-up to death				
Cause of death	*0-5 years (n=3080)**	*6-10 years (n=2373)*	*11-20 years (n=1689)*	*21-29 years (n=584)*	*Total (n=3080)*
Initial SAH and sequelae	41 (21%)	27 (15%)	15 (6%)	4 (6%)	87 (12%)
Rebleeding (same aneurysm)	8 (4%)	5 (3%)	5 (2%)	0 (0%)	18 (3%)
Another aneurysm ruptured	5 (3%)	4 (2%)	4 (1%)	4 (6%)	17 (2%)
Cerebrovascular	13 (7%)	20 (11%)	45 (17%)	7 (11%)	85 (12%)
Cardiovascular	42 (22%)	52 (28%)	77 (28%)	14 (22%)	185 (26%)
Cancer	40 (21%)	38 (21%)	59 (22%)	18 (28%)	154 (22%)
Trauma	9 (5%)	8 (4%)	10 (4%)	4 (6%)	31 (4%)
Suicide	7 (4%)	4 (2%)	3 (1%)	0 (0%)	14 (2%)
Other	21 (11%)	23 (13%)	51 (19%)	14 (22%)	109 (15%)
Not known	5 (3%)	4 (2%)	3 (1%)	1 (2%)	13 (2%)
Total number of deaths	191 (100%)	185 (100%)	272 (100%)	65 (100%)	713 (100%)

* Patients at risk, total number of SAH patients at the beginning of follow-up period

Excess in Long- Term Mortality

There was constant excess mortality throughout the whole study period in study population compared to matched general population. Cumulative RSR was 0.94 (95% CI 0.93 – 0.95) at 10 years, 0.82 (95% CI 0.79-0.85) at 20 years and 0.75 (95% CI 0.70 – 0.81) at 28 years indicating excess mortality of 6%, 18% and 25% respectively. Cumulative relative survival ratios (RSRs) are presented in Figure 1.

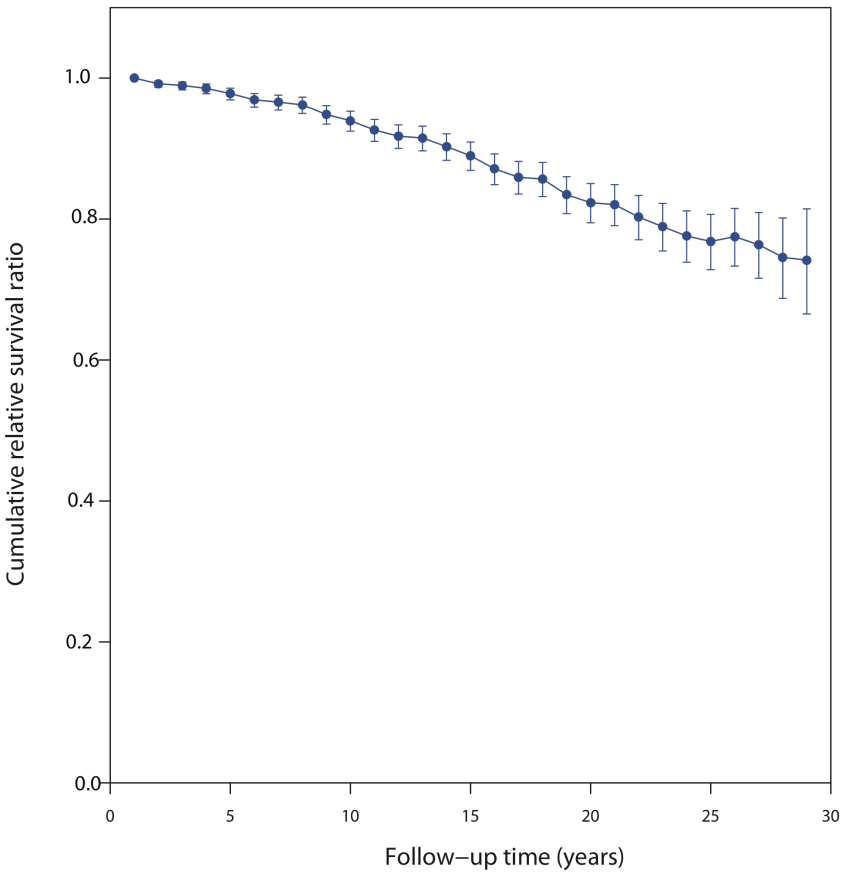

Figure 1

Cumulative relative survival ratio (CRSR) of 3080 patients with ruptured saccular aneurysm compared to matched general population as a function of time.

Risk Factors of Long- Term Excess Mortality

Age

Patients who were over 60 years old (n=583) had markedly higher excess mortality (10-year cumulative RSR 0.89, 95% CI 0.83 - 0.94, 20-year cumulative RSR 0.64, 95% CI 0.51 – 0.78) than patients aged 44 or younger (n=1208, 10-year cumulative RSR 0.96 95% CI 0,94 – 0,97, 20-year cumulative RSR 0.88, 95% CI 0.85 – 0.91).

Even the youngest age group, patients aged 44 or younger, had significant excess long-term mortality (25-year cumulative RSR 0.84, 95% CI 0.80 – 0.88) compared to matched general population. Of these younger patients, who died during the follow-up, 95% died before the age of 65. The patients aged 44 or younger seemed to have excess mortality caused by sequelae of SAH (n=37), cardiovascular disease (n=39) and cerebrovascular disease (n=14) accounting 20%, 21% and 8% of all causes of death respectively.

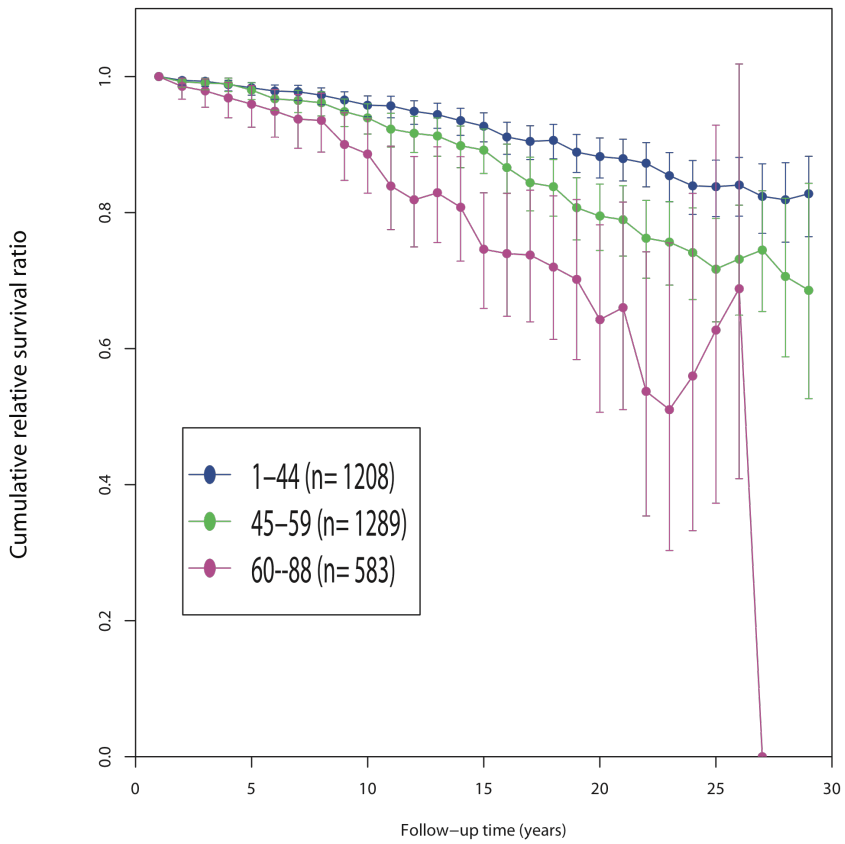

Figure 2

Cumulative RSRs as a function of follow-up time for three age groups: ≤44 years (blue), 45–59 years (green), and ≥60 years (purple).

Multiple Aneurysms

Patients with a single aneurysm had better survival (n=2177, 25-year cumulative RSR 0.82, 95% CI 0.78 – 0.87) than patients with multiple aneurysms (n=903, 25-year cumulative RSR 0.63 , 95% CI 0.55 – 0.71). New and lethal subarachnoid hemorrhage from another aneurysm was more common among patients with multiple aneurysms than in single aneurysm group (n=9, 20% vs. n=8, 15% of patients with SAH as the main cause of death).

The portion of lethal rebleedings before treatment or from previously treated aneurysm was also slightly higher in multiple aneurysm group (n=9 vs. n=9 among single aneurysm patients , 20% and 17% of SAH related deaths). Other vascular causes of death were not overrepresented among multiple aneurysm patients: cardiovascular disease 24% vs. 27% in single aneurysm group and cerebrovascular causes 12% vs. 13 % respectively. Cumulative relative survival ratios (RSRs) are shown in figure 3.

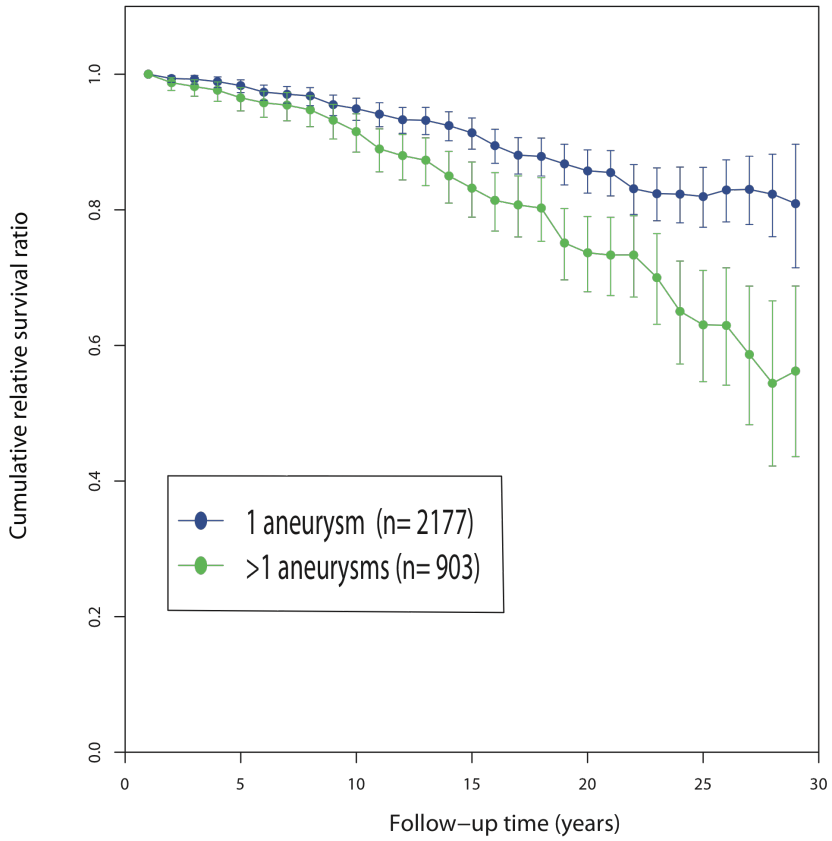

Figure 3

Cumulative RSRs as a function of follow-up time for patients with multiple aneurysms (green) and patients with a single aneurysm (blue).

Preoperative Clinical Condition

Preoperative clinical condition (HH/WFNS) was related to long-term survival. Patients with severe neurological impairments before treatment had significantly higher excess long-term mortality than patients with mild symptoms. Patients who had excess mortality within the first five-year period were mainly in poor preoperative clinical condition, HH grades 4 and 5. Later on, patients with good preoperative condition also started to show clear excess mortality. The cumulative RSR at 20 years of follow-up for HH 1: 0.91 (95% CI 0.86 – 0.95), for HH 2: 0.86 (95% CI 0.81 – 0.90), for HH 3: 0.72 (95% CI 0.65 – 0.78), for HH 4: 0.73 (95% CI 0.62 – 0.83) and for HH 5: 0.49 (95%CI 0.19 - 0.77).

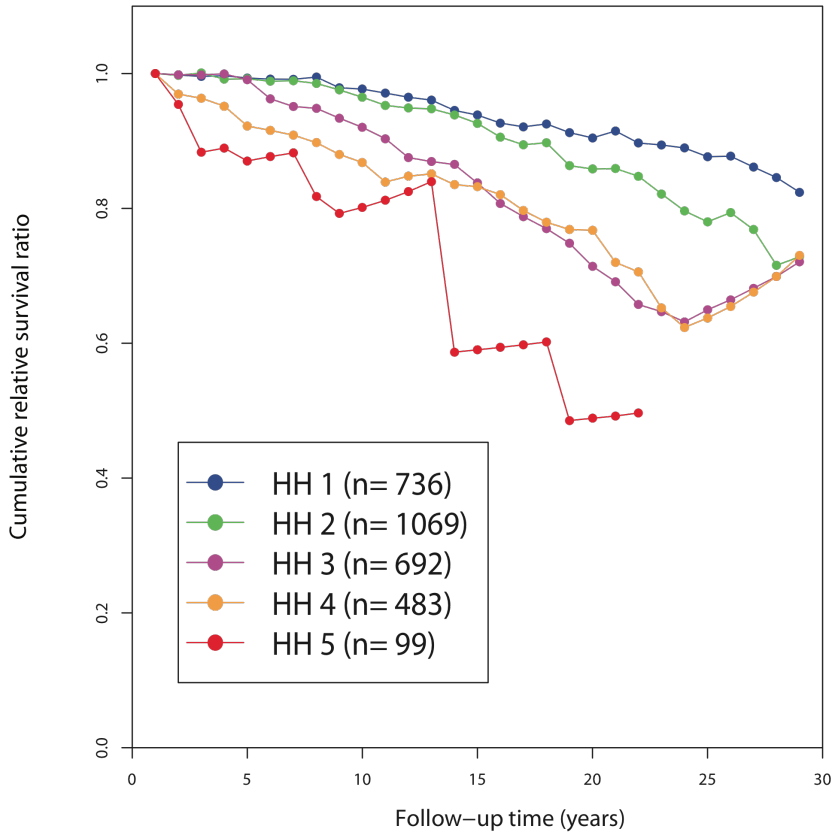

Figure 5
Cumulative RSRs according to patients´ preoperative clinical condition (Hunt & Hess grade) and as a function of time.

Conservative Treatment

Considering all the aneurysmal SAH patients (n=4228) who got treatment between 1980 and 2007, total of 414 patients were treated conservatively. Most of the them (n=368, 89%) died within the first year after the SAH. At one year, only 46 (11%) of the conservatively treated patients were alive. Conservative treatment resulted in significantly impaired long-term survival, cumulative RSR at 25 years 0.38 (95% CI 0.20 – 0.59), in comparison to patients with actively treated aneurysm having 25-year cumulative RSR 0.78 (95% CI 0.74 – 0.82).

Conservatively treated patients were mainly in worse clinical condition at admission to the hospital (Hunt & Hess 4-5 43%, Hunt & Hess 3 33%) than patients who were operated (Hunt & Hess 4-5 19%, Hunt & Hess 3 22%). They also had relatively more lethal rebleedings than patients with operated aneurysms (n=5, 33% vs. n=13, 16% of patients with SAH as the main cause of death).

Aneurysm Location and Gender

Aneurysm location did not have impact on long-term survival. During the first year after SAH greater portion of SAH patients with aneurysm of posterior circulation died than patients with aneurysms of other locations. Later on, there were not significant differences between groups; in the long run, cumulative RSRs of all loci showed excess mortality (Figure 6).

Patients' gender did not affect long-term excess mortality: 10-year cumulative RSRs 0.94 (95% CI 0.92- 0.95) for women and 0.94 (95% CI 0.92- 0.96) for men, 20-year cumulative RSRs 0.82 (95% CI 0.78- 0.85) for women and 0.84 (95% CI 0.79- 0.88) for men.

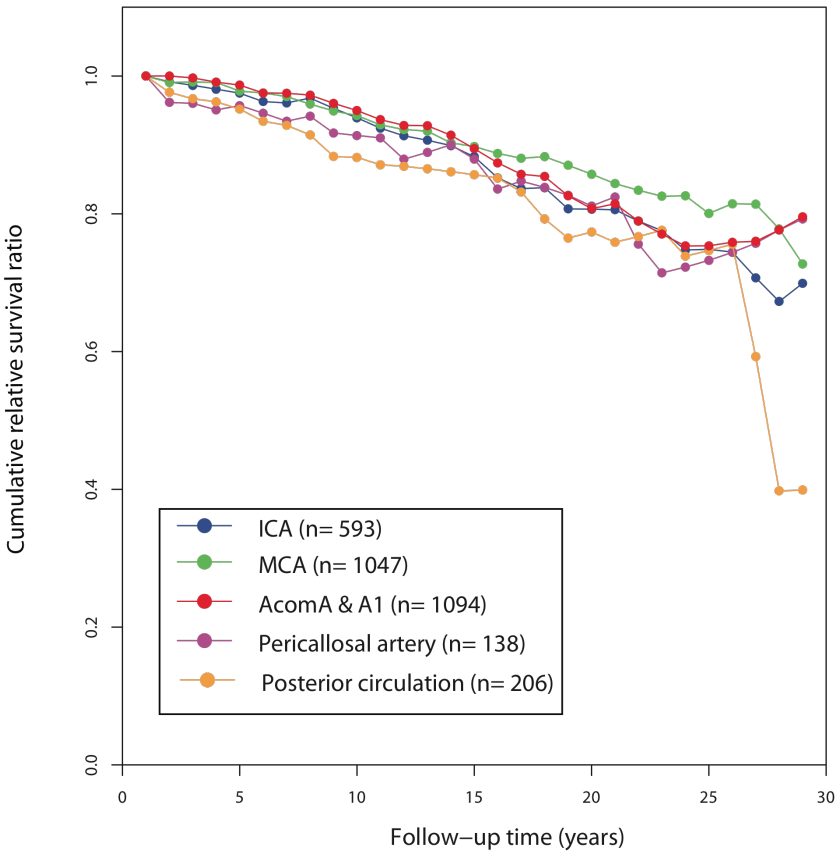

Figure 6

Cumulative RSRs of SAH patients, divided into groups according to the location of ruptured aneurysm and presented as a function of time.

Outcome at 3 months

As expected, patients who had serious disabilities at three months after SAH also had greater long-term excess mortality when compared to patients with good recovery according to Glasgow outcome score (Figure 7). Considering patients with GOS 2, 67% of them died because of SAH.

Remarkably, patients with good recovery after the SAH also had notable excess in long-term mortality but they did not start to show it until after 8 years of follow-up (25-year cumulative RSR for GOS 5 0.85, 95% CI 0.80-0.90). Patients with good recovery at 3 months had cardiovascular disease (31%) and cancer (27%) as the leading causes of death. They had the lowest portion of deaths caused by SAH (9% GOS 5 vs. 12% GOS 4 and 20% GOS 3).

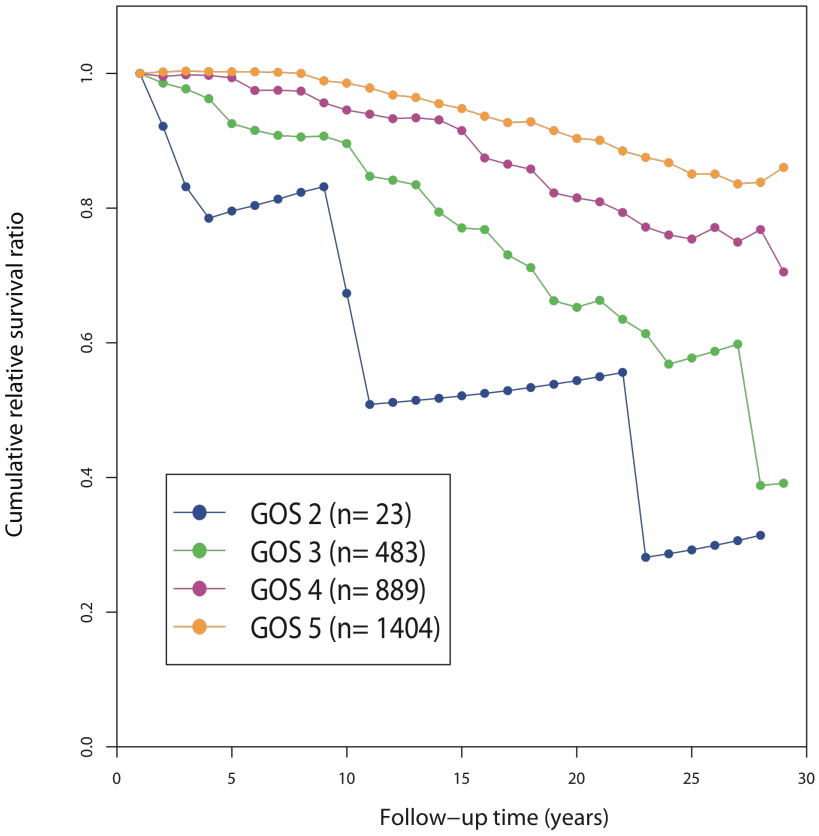

Figure 7

Cumulative RSRs as a function of time according to patients´ clinical outcome at 3 months after SAH: GOS 5 Good Recovery (yellow), GOS 4 Moderate Disability (purple), GOS 3 Severe Disability (green) and GOS 2 Persistent vegetative state (blue).

4 Discussion

In this follow-up study of 3080 aneurysmal SAH patients, there was constant excess mortality throughout the whole study period. The cumulative relative survival ratios showed 18% excess mortality at 20 years compared to the matched Finnish general population. Even young patients and patients with good recovery showed excess mortality in the long run. The excess mortality became more obvious after ten years of follow-up and was highlighted during the following decades. The advantages of this study were: (a) exceptionally large number of study patients; (b) extensive follow-up of nearly 37 000 patient-years; (c) low number of excluded patients in comparison to the whole study group and (d) detailed population registers and mortality statistics in Finland, which include all Finnish residents. The fact that this is a retrospective follow-up study caused some selection bias that needs to be considered when looking at the results.

Long-term Mortality after SAH

So far, there is only limited knowledge on the long-term follow-up of aneurysmal SAH patients. Most studies report outcome at relatively early phase of recovery, most often three to 12 months after the SAH (2,8,17,18) There are very few studies which address patients' outcome more than five years after the initial SAH (1,9-12). The general belief has been, that after successful recovery, SAH should have no further effect on patients' survival. However, what some studies have shown is, that despite surviving the initial aSAH, many of the patients die earlier than their peers (1,9,11,12).

In earlier Finnish study of 1537 SAH patients by Ronkainen et al. it was suggested that aneurysmal SAH might be a manifestation of general vascular disease (9). The study by Wermer et al. from the Netherlands suggested that treatment of cardiovascular risk factors should be considered due to elevated incidence of vascular events (11). The most common causes of death in our study group were cardiovascular disease (26%) and cancer (22%). Among patients with good recovery at 3 months, these were highlighted as the leading causes of death (31% and 27% respectively). Patients younger than 65 years had cardiovascular disease as the leading cause of death (24%). In the general Finnish

population lethal cardiovascular events are less frequent in under 65-year-old Finns (19% in men and 7% in women) but common in over 65-year-old Finns (28%) (19). This indicates that SAH patients have increased mortality due to cardiovascular disease at younger age. The increased risk of cardiovascular disease may be due to general cardiovascular disease, the impact of SAH on the cardiovascular system or due to the shared risk factors like elevated blood pressure and smoking. Our results suggest that the treatment of cardiovascular risk factors should be emphasized on patients younger than 65.

Deaths caused by cerebrovascular disease were also overrepresented among our study patients (15% for ≥ 65 years, 8% < 65 years) compared to general Finnish population (11% for ≥ 65 years, 6% < 65 years) (19). A significant cause of mortality were sequelae of the initial SAH. They counted about one fifth of all deaths in the first five- year period but were less prominent later on. It is possible that long-term rehabilitation and follow-up of SAH patients is not optimal nowadays. The effects and disabilities caused by SAH may not be paid enough attention to in the years following SAH, which may increase morbidity and mortality.

The risk of lethal recurrent SAH was not high but remained elevated after primary SAH. Long-term risk of rebleeding from previously treated aneurysm seemed to be greatest during the first five- year period of follow-up and decreased after that. The risk of new, lethal SAH from another aneurysm did not lower in a long run. It was higher among patients with multiple aneurysms than among patients with a single aneurysm. The total risk of lethal, recurrent SAH was about three times as high as the risk of SAH striking for the first time.

Long-term Excess Mortality

There are only five publications on long-term mortality of aneurysmal SAH patients (1,9-12). Three of these studies come from Finland, one from Iceland and one from the Netherlands, indicating how difficult it is to carry out a reliable long-term follow-up study. The results are partly contradicting, especially when it comes to survival of young patients and the patients with good recovery after SAH.

In our study, the total cumulative relative survival ratios showed 18% excess mortality at 20 years compared to matched general Finnish population (cumulative RSR 0.82, 95% CI 0.79- 0.85). The latest population-based study of 1746 one-year survivors of SAH in Eastern Finland with median follow-up 12 years showed 12% excess mortality at 15 years compared to matched general population (cumulative RSR 0.88, 95% CI 0.85- 0.91) (12). These findings are similar, both presenting significant long-term excess mortality after SAH. Eventhough both of these studies are from Finland, the method of calculating RSRs, using matched general population, should fade the effect of the population it is based upon and describe only the effect of SAH.

Risk Factors for Excess Mortality

Risk factors for long-term excess mortality turned out to be: age (especially above 60 years); poor preoperative clinical condition; conservative treatment; multiple aneurysms; and unfavourable clinical outcome at 3 months after the SAH.

Age

The patients aged 60 and older were in the greatest risk of dying earlier than their fellow citizens according to our series. This is in line with the recent study of Huttunen et al. in which age above 64 years was an independent risk factor for long-term excess mortality (12). In the Dutch study of 752 SAH patients by Wermer et al., young patients had the highest excess mortality and earlier study by Ronkainen et al. suggested the same (9,11). In our study, age group of 60-88 showed the highest excess mortality. But, there was significant excess mortality of 16% at 25-years of follow-up even in our youngest age group (1-44 years). These patients died at ages much younger than their peers, with

sequelae of the initial SAH, cardiovascular and cerebrovascular disease representing half of all the causes of death.

Preoperative Clinical Condition

It was expected that poor preoperative clinical condition leads to impaired survival. Surprisingly, even patients with good preoperative clinical condition showed excess mortality during follow-up. This was seen in using both HH and WFNS grading scales. There was excess mortality of 9% at 20 years for patients with HH 1 and 14% at 20 years for patients with HH 2. Similar results were seen in the study of Huttunen et al. who reported 11% excess mortality at 15 years for patients with HH 1-2 on admission (12).

Conservative Treatment

The conservatively treated patients had markedly higher excess mortality than patients who got active treatment. The selection bias, related to this study, affects especially allocation into these two treatment groups. The conservative treated patients were initially in worse clinical condition and were expected to have worse prognosis in comparison to actively treated patients. In addition, 89% of the conservatively treated patients died during the first year of follow-up, as compared to the 14% of actively treated.

Multiple Aneurysms

We got new information concerning the prognosis of the patients with multiple aneurysms. They had not only higher excess mortality but also increased risk of dying due to rupture of another aneurysm than patients with just single aneurysm. It is not known if treating all the aneurysms early enough will decrease their mortality but this is something we would like to study in the future. It is possible that patients with multiple aneurysms have more severe general vascular disease, and multiplicity of aneurysms is just a representation of the severity of the disease. When looking at causes of death this can not be verified; cardiovascular disease (27% for single aneurysm group, 24% for multiple aneurysm patients), and cerebrovascular disease (13% and 12% respectively).

Clinical Outcome at 3 Months

It has been a generally accepted belief, that after good recovery, SAH patients should have the same life expectancy as other people. An Icelandic study of only 44 SAH patients showed no excess mortality among patients with good recovery at 6 months (1). Also in a Finnish series of 280 ruptured distal anterior cerebral artery aneurysm patients, there was no long-term excess mortality for patients with good recovery at 12 months (10). The first study was limited by a small number, whereas in the latter one certain distinct features of

the distal anterior cerebral artery aneurysms such as their frontal and cortical location, may explain the relatively better outcome when compared to all aneurysm locations. Our results seem to be in line with the other two larger studies which included all aneurysm sites. They reported excess mortality (9% or twice that of the general population) even in patients with initial good recovery (9,12). In our study, patients with good recovery at 3 months showed 15% cumulative excess mortality in 25-year follow-up. The excess mortality was not clearly seen during the first ten years but became evident after that. So, contrary to the general belief, even patients with good initial recovery after aSAH are burdened by their SAH experience and die earlier than matched population.

Gender and Location of Aneurysm –No Related Risk

Gender or location of the ruptured aneurysm had no effect on long-term survival according to our data. These results are not supported by the study of Huttunen et al., which suggested that male sex and basilar tip aneurysms were related to long-term excess mortality (12). In our study the mortality related to basilar tip aneurysms was elevated during the first year after the SAH but later on it did not differ from the mortality of the patients with aneurysms at other locations.

5 Conclusions

Despite initial good recovery aneurysmal SAH patients are burdened by the SAH in the long run. They show significant long-term excess mortality when compared with matched general population. Risk factors for excess mortality are old age, poor preoperative clinical condition, conservative aneurysm treatment, multiple aneurysms and unfavourable clinical outcome at 3 months after SAH. Cardiovascular disease at younger age and cerebrovascular events are overrepresented as causes of death, which indicates the importance of treatment of cardio- and cerebrovascular risk factors after SAH.

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